REMARKS

The office action dated January 29, 2007 has been received and noted. Claims 1, 3, 7, 8, 10-12 and 14-16 were examined. Claims 1, 3, 7, 8, 10-12 and 14-16 were rejected. Claims 1, 11 and 14 are amended. Claim 15 is cancelled. Support for the new claims and for the amendments can be found in, for example, page 3, lines 28-30 of the Application. As such, no new matter has been added. Claims 1, 3, 7, 8, 10-12, 14 and 16 remain in the Application. Reconsideration of the pending claims is requested in view of the above amendments and following remarks.

I. Claim Objections

Claims 1 and 14 were objected to due to informalities. Appropriate correction has been made.

II. Claims Rejected under 35 U.S.C. § 112

Claim 11 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. More specifically, the Examiner objects that claim 11 depends from a cancelled claim. Amended claim 11 now depends from claim 1. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

III. Double Patenting

Claims 1, 3, 7, 8 and 14-16 have been provisionally objected on the ground of non statutory double patenting over claims 1-12 of co-pending U.S. Application No. 10/753,417. Applicants hold in abeyance any response to the Examiner's provisional obviousness-type double patenting rejection pending the outcome of the claims and until such time as the rejection becomes non-provisional.

IV. Claims Rejected under 35 U.S.C. § 103

A. Claims Rejected as Unpatentable over *Merlino* in view of *Felten*

Claims 1, 10, 11, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over *New chromogenic identification and detection of Staphylococcus aureus and methicillin-resistant S. aureus* to Merlino et al. ("*Merlino*") in view of *Evaluation of three techniques for detectionof low-level methicillin-resistant Staphylococcus aureus (MRSA): a disk diffusion method with cefoxitin and moxalactam* to *Felten* et al. ("*Felten*"). In order to establish a *prima facie* case of obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference; (2) there must be a reasonable expectation of success; and (3) the references when combined must teach or suggest all of the claim limitations. MPEP § 2142. Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Amended independent claim 1 includes the limitation of "[a] culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase." (App., claim 1.) Similarly, amended independent claim 14 includes the limitation of "[a] method of detecting methicillin-resistant *Staphylococci aureus* (MRSA) in a sample from a patient." (App., claim 14.) Moreover, both claims 1 and 14 include the limitation of an antibiotic incorporated ***within*** the culture medium. (App., claims 1, 14.)

By contrast, *Merlino* is directed to a chromogenic plate medium for identification of *Staphylococcus aureus* on the basis of colony pigmentation. (*Merlino*, Abstract.) As recognized by the Examiner, *Merlino* does not teach the use of the claimed cephalosporin antibiotics as selective agents in a chromogenic medium, much less incorporated within the plate medium. (Office Action, p.5.) Moreover, *Merlino* does not teach or suggest that the plate medium is adapted to detect *Staphylococcus aureus* directly from direct clinical specimens. (*Merlino*, p.2380, ¶ 2.) *Felten* is directed to three methods for detection of low-level MRSA, including the ***disk diffusion method***, the Vitek 2 system and the MRSA-screen test. (*Felten*, Abstract.) According to *Felten*, before any of the methods are used for MRSA detection, S. aureus ***isolates*** are prepared into a high density inocula, which is a liquid solution. (*Felten*, p.2767.) Then, the "entire surface" of the agar plate is covered with the inocula. It is only after this process that the methods described in *Felten* are employed. (*Id.*) Furthermore, the agar plate is disclosed to be a

standard MHA plate, which ***does not*** include an antibiotic incorporated therein. (*Id.*) Instead, a disk having a cephamycin antibiotic is placed ***on the surface of the agar plate*** for the disk diffusion method in order to detect MRSA. (*Id.*)

Thus, the cited references do not teach or suggest all of the claim limitations of independent claims 1 and 14, namely, "a culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase." Instead, the cited references are directed to *S. aureus* isolates, which isolates correspond to homogenous bacterial populations, which are very different from a sample of a patient, directly or after an enriching phase, and which sample comprises heterogenous bacterial populations. Also, the cited references do not teach or suggest that an antibiotic is incorporated within the plate mediums.

Moreover, taking into account secondary considerations, Applicants' claimed invention is not obvious. *See Graham v. John Deere Co.*, 383 U.S. 1 (1966). Applicants' claimed invention evidences a long-felt need for a cost-effective and quick method for identifying nosocomial MRSA. In support thereof, the specification states "[t]he medium according to the invention makes it possible in particular to readily detect met[h]icillin-resistant staphylococci, while reducing the analysis time." (App., p. 10, lns. 16-18.) Additionally, the Tande 2003 reference establishes the advantages of Applicants' claimed invention by describing a specificity of 100% and a sensitivity of 98% in detecting MRSA directly from swabs of patients with the culture medium of CHROMagar (identification tests include Gram colouration, catalase and agglutination, but not a chromogenic agent that releases a chromophore after hydrolysis with an enzyme that is active). Additionally, at least one Examiner-cited reference supports this long-felt need: "Reliable and rapid methods to identify [MRSA] are crucial in any clinical laboratory." (*Merlino*, p.2378.)

In view of the above Remarks, Applicants submit that independent claims 1 and 14 and their respective dependent claims are allowable over the cited references.

B. Claims Rejected as Unpatentable over *Merlino* in view of *Felten* and in view of *Boggs*

Claims 1, 10-12, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Merlino* in view of *Felten* and in view of U.S. Patent No. 5,883,074 to Boggs et al. ("*Boggs*"). Applicants respectfully submit that the cited references do not teach or suggest all of the claim limitations of independent claims 1 and 14. As a preliminary matter, *Merlino* in view of *Felten* do not teach or suggest all of the claim limitations of claims 1 and 14 for the reasons stated in section IV(A) of this Response.

Boggs is directed to a method of treating bacterial infections using small molecules, termed potentiators. (*Boggs*, col. 3, lns. 50-53.) The potentiators, which exhibit little or no antibacterial activity, can be used to induce susceptibility to an anti-bacterial agent in a bacterium resistant to that agent when used in conjunction with the anti-bacterial agent. (*Boggs*, col. 3, lns. 52-58.) The screening process for detecting possible potentiator candidates includes testing the candidates in a microtiter plate which includes a liquid suspension of MRSA cells, the potentiator candidate, and methicillin. (*Boggs*, Ex. 1.) According to *Boggs*, the anti-bacterial agent can be "a β-lactam, a β-lactam mimic, a glycopeptide, a macrolide, a quinolone, a tetracycline, or an aminoglycoside." (*Boggs*, col. 6, lns. 16-25.) *Boggs* further teaches that in preferred embodiments, the anti-bacterial agent can be "ampicillin, amoxicillin, cloxacillin, flucloxacillin, methicillin, oxacillin, piperacillin, azlocillin, mezlocillin, cefaclor, cefalexin, cefamandole, cefazolin, cefonicid, cefoperazone, cefotaxime, cefoxitin, ceftazidime, cefpirome, ceftriaxone, cephalothin, ceftibuten, cefixime, cefpodoxime, imipenem, meropenem, mezlocillin, loracarbef, fluoxacillin, dicloxacillin, cefmenoxime, cefotiam, cefotetan, or biapenem." (*Boggs*, col. 6, lns. 16-25.)

Independent claims 1 and 14 inherently teach that MRSA may be resistant to one of cefamandole, cefoxitin, cefmetazole, moxalactam, cefotetan and flomoxef, as any one of these anti-bacterials may be added to the culture medium to detect MRSA, i.e., MRSA may grow despite the presence of the particular anti-bacterial thus indicating resistance. (*See* App., p.11, ln. 32 through p.12, lns. 1-2.) Thus, *Boggs* teaches that cefamandole, cefotixin or cefotetan must be combined with a potentiator in order to induce susceptibility in resistant bacteria, and does not therefore teach or suggest that MRSA are often selectively resistant to the anti-bacterials cefamandole, cefotixin or cefotetan alone. As such, in addition to failing to teach or suggest all of the limitations of independent claims 1 and 14 (as do *Merlino* and *Felten*), Applicants submit that *Boggs* teaches away from combination of the cited references, thereby failing to supply the

required motivation to combine *Boggs* with *Merlino* and *Felten* to arrive at Applicants' claimed invention.

Additionally, Applicants are unable to discern anywhere in *Boggs* the limitation of "[a] culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase," as recited in claims 1 and 14. As such, and in view of the remarks in section IV(A) of this Response, the cited references do not teach or suggest all of the limitations of claims 1 and 14 in view of this further limitation. Accordingly, Applicants submit that independent claims 1 and 14 and their respective dependent claims are allowable over the cited references.

C. Claims Rejected as Unpatentable over *Merlino* in view of *Felten* and in view of *Dorso*

Claims 1, 10-12, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Merlino* in view of *Felten* and in view of U.S. Patent No. 6,221,859 to Dorso et al. ("*Dorso*"). Applicants respectfully submit that the cited references do not teach or suggest all of the claim limitations of independent claims 1 and 14. As a preliminary matter, *Merlino* in view of *Felten* do not teach or suggest all of the claim limitations of claims 1 and 14 for the reasons stated in section IV(A) of this Response.

Dorso is directed to 2-(naphthosultamyl) methyl-carbapenaem antibacterial agents in combination with β-lactams to treat enterococcal infections caused by MRSA, MRSE and MRCNS. (*Dorso*, Abstract.) The β-lactams can include "carbapenems such as imipenem (plus or minus cilastatin; with cilastatin=Primaxin®), meropenem, biapenem, panipenem, (4R,5S,6S)-3-[3S,5S)-5-(3-carboxyphenylcarbamoyl)pyrrolidin-3-ylthio]-6-(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, an enantiomer, diastereomer or pharmaceutically acceptable salt thereof and the like, cephalosporins and cephamycins such as cefoperazone, cefotiam, cefpirome, cefmetazole, cafazolin, cephalexin, cefuroxime, cefaclor, cefotaxime, ceftriaxone, moxalactam, cefixime and the like and penicillins such as ampicillin, amoxicillin, piperacillin, nafcillin, oxacillin, cloxacillin and combinations of penicillins with a beta-lactamase inhibitor such as sulbactam, clavulanic acid, tazobactam, and the like." (*Dorso*, col. 8, ln.63 – col. 9, ln. 10.) The bacteria culture is obtained from "stock cultures" and grown in centrifuge tubes. (*Dorso*, Ex. 1.)

Independent claims 1 and 14 inherently teach that MRSA may be resistant to one of cefamandole, cefoxitin, cefmetazole, moxalactam, cefotetan and flomoxef, as any one of these anti-bacterials may be added to the culture medium to detect MRSA, i.e., MRSA may grow despite the presence of the particular anti-bacterial thus indicating resistance. *Dorso* teaches that cefmetazole must be combined with 2-(naphthosultamyl) methyl-carbapenaem antibacterial agents in order to be effective, and does not therefore teach or suggest that MRSA are often selectively resistant to the anti-bacterial cefmetazole. Moreover, Applicants respectfully disagree with the Examiner's characterization of *Dorso* that "[Dorso] teach[es] that cefmetazole is among the antibiotics that are losing efficacy against pathogenic bacteria, and must be combined with other compounds to enhance treatment." (Office Action, p.7.) In fact, in the context of efficacy, *Dorso* only teaches that:

> [t]he claimed compositions contain antibiotic agents which are of the broad class known as carbapenems . . . [many of which] are susceptible to attack by a renal enzyme known as dehydropeptidase (DHP). This attack or degradation may reduce the efficacy of the carbapenem antibacterial agent. Many of the compounds of the present invention, on the other hand, are less subject to such attack, and therefore may not require the use of a DHP inhibitor

and does not disclose any experimental results which indicate that the anti-bacterial cefmetazole is selectively resistant. (*Dorso*, col. 15, lns. 1-8.) As such, in addition to failing to teach or suggest all of the limitations of independent claims 1 and 14 (as do *Merlino* and *Felten*), Applicants submit that *Dorso* teaches away from combination of the cited references, thereby failing to supply the required motivation to combine *Dorso* with *Merlino* and *Felten* to arrive at Applicants' claimed invention.

Additionally, Applicants are unable to discern anywhere in *Boggs* the limitation of "[a] culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase," as recited in claims 1 and 14. As such, and in view of the remarks in section IV(A) of this Response, the cited references do not teach or suggest all of the limitations of claims 1 and 14 in view of this further limitation. Accordingly, Applicants submit that independent claims 1 and 14 and their respective dependent claims are allowable over the cited references.

D. Claims Rejected as Unpatentable over *Merlino* in view of *Felten* and in view of *Hanaki*

Claims 1, 10-12, 14 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Merlino* in view of *Felten* and in view of U.S. Patent No. 6,294,527 to Hanaki ("*Hanaki*"). Applicants respectfully submit that the cited references do not teach or suggest all of the claim limitations of independent claims 1 and 14. As a preliminary matter, *Merlino* in view of *Felten* do not teach or suggest all of the claim limitations of claims 1 and 14 for the reasons stated in section IV(A) of this Response.

Hanaki is directed to cepham derivative compounds effective for MRSA and VRE. (*Hanaki*, Abstract.) Applicants are unable to discern anywhere in *Hanaki* the limitation of "[a] culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase," as recited in claims 1 and 14. As such, and in view of the remarks in section IV(A) of this Response, the cited references do not teach or suggest all of the limitations of claims 1 and 14 in view of this further limitation. Accordingly, Applicants submit that independent claims 1 and 14 and their respective dependent claims are allowable over the cited references.

E. Claims Rejected as Unpatentable over *Merlino* in view of *Felten* and in view of *Rambach*

Claims 1, 3, 7, 8, 10-12 and 14-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Merlino* in view of *Felten* and in view of U.S. Patent No. 6,548,268 to Rambach ("*Rambach*"). Applicants respectfully submit that the cited references do not teach or suggest all of the claim limitations of independent claims 1 and 14. As a preliminary matter, *Merlino* in view of *Felten* do not teach or suggest all of the claim limitations of claims 1 and 14 for the reasons stated in section IV(A) of this Response.

Rambach is directed to the use of 5-bromo-6-chloro-3-indoxyl phosphate and 5-bromo-4-chloro-3-indoxyl glucoside as color agents to detect *S. aureus*. (*Rambach*, Abstract.) Applicants are unable to discern anywhere in *Rambach* the limitation of "[a] culture medium for detecting methicillin-resistant *Staphylococci aureus* (MRSA) directly from a sample from a patient or after an enriching phase," as recited in claims 1 and 14. As such, and in view of the remarks in section IV(A) of this Response, the cited references do not teach or suggest all of the limitations of

claims 1 and 14 in view of this further limitation. Accordingly, Applicants submit that independent claims 1 and 14 and their respective dependent claims are allowable over the cited references.

CONCLUSION

In view of the foregoing, it is believed that all claims now pending, namely claims 1, 3, 7, 8, 10-12 and 14-16, and are in condition for allowance and such action is earnestly solicited at the earliest possible date. If the Examiner believes that a telephone conference would be useful in moving the application forward to allowance, the Examiner is encouraged to contact the undersigned at (310) 500-4787.

Respectfully submitted,

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CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being submitted electronically via EFS Web to the United States Patent and Trademark Office on April 30, 2007.

Suzanne Johnson 4/30/07